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An Approach to the Toxicology of Combustion Products of Materials*

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Physiological and behavioral (conditioned avoidance) responses of male Long-Evans rats were determined during exposure to combustion products produced on thermal degradation of three different polymeric materials. Arterial blood samples were obtained for determination of carboxyhemoglobin (COHb) and acid/base status. Material A produced a syndrome of carbon monoxide (CO)-induced anoxia, the severity of which was a function of the mass of material degraded. Material B produced *grand mal* seizures despite COHb levels of less than 10%. Material C produced metabolic acidosis and a mild degree of CO-induced anoxia. Loss of avoidance responses occurred at significantly lower COHb levels for materials B and C in comparison to CO alone. Using responses to COHb as a reference, it was possible to detect the presence of other toxicants present in combustion products. Compounds found in smoke in very low concentrations may have a high degree of biological activity and be responsible for impairment of survival responses. We have labeled these compounds "limiting" toxicants. They constitute a significant hazard, which is added to that of CO and anoxia.

Introduction

When a material is decomposed by a process of combustion or pyrolysis, the combustion products comprise a mixture of substances. This fact presents a significant problem to those interested in the evaluation of animal or human response to such products. It is difficult to establish whether the intoxication syndrome (the signs and symptoms of intoxication consistently produced on exposure to the combustion products) is produced as a consequence of the action of one, some, or all of the substances present in the smoke. Since both quantitative and qualitative changes in combustion products occur when the mode of decomposition is changed (flaming vs. nonflaming), the intoxication syndrome is also expected to vary with these parameters. The problem becomes even more complicated when one considers combinations of materials in attempting to relate observations concerning toxicity to some idealized "real" fire situation.

Fire safety standards for materials have largely ignored the complexity of the problem and are grossly over-simplified. Ratings for flammability are sometimes confused with those for toxicity. Statements such as "shall be no more toxic than wood," used in recently adopted codes (*1*), are virtually meaningless in view of the paucity of information available on toxic responses to the combustion products of wood. The present situation is confused and may even be described as chaotic. It is important that the objectives for the evaluation of toxicity of combustion products be clearly stated.

The results of chemical analysis of the combustion products of a great number of materials at varying heat fluxes in both flaming and nonflaming modes have disclosed several important factors. First, because of the great number of products, it may not be possible to determine which one of them is responsible for a given toxic effect. Second, the biological

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activity of a compound may make it of great importance in the production of the intoxication syndrome, but its concentration may be very low, or it may not even be detectable by customary techniques. Third, as the mode of decomposition is changed, qualitative changes in combustion products occur. Such changes may or may not have an effect upon the qualitative nature of the intoxication syndrome.

It is also evident that certain generalizations, simplifications, and approximations must be made to provide useful criteria at an early stage of development of test protocols and methodology. It is most reasonable to emphasize those factors which limit survival, rather than those surrounding the event of death.

Once objectives for evaluation of toxicity are stated and data are derived in order to fulfill these objectives, then it may be possible to classify materials in terms of their relative toxicity. This evaluation must then be considered in relation to material use and flammability characteristics. Ideally, as new materials are developed, criteria for toxicity assessment should be fulfilled prior to large-scale production and use. This principle, i.e., assessment of toxicity prior to use, should be applied to all new materials before they enter our environment.

Objectives for Assessment of Toxicity

Description of the Intoxication Syndrome

A syndrome is defined as that collection of signs and symptoms characteristically occurring when an organism (usually man) encounters a specific noxious agent or condition in its environment. An intoxication syndrome is that syndrome produced on exposure to a specific toxicant. Exposure to the combustion products of a specific material may produce a characteristic syndrome. It is essential to describe fully the nature of this syndrome and to determine the toxicant responsible for the effects that are seen. This requires monitoring of physiological, biochemical, and behavioral parameters, so that significant alterations in organ-system function can be detected as soon as they occur. We have used a sling-restrained Long-Evans male rat and have monitored electrocardiogram (EKG), electroencephalogram (EG), respiratory rate (RR), and blood pressure (BP) and have used such measurements as peripheral nerve conduction velocity (ventral caudal nerve) and visual evoked response when indicated by specific effects of intoxication. An intra-arterial cannula should be used for continuous and frequent measurements of the state of blood oxygenation, acid base balance, and assessment of organ or muscle involvement by measurement of serum enzymes.

The sling restraint permits simultaneous physiological and behavioral assessment. We have used a standard conditioned avoidance response, which consists of left-hind limb flexion avoidance of a shock delivered from a plate set a standard distance from the foot.

By using the rat as a model for the study of intoxication and with instrumentation of this type, it is possible to define rather clearly the various alterations that occur during developing intoxication on exposure to a mixture of combustion products. These physiological and behavioral measures will describe the intoxication syndrome with respect to a number of parameters.

Mechanism of Intoxication and the Concept of Limiting and Graded Toxicants

The most common syndromes associated with exposure to combustion products are those resulting from impaired oxygen delivery or transport, i.e., anoxic anoxia (resulting from impaired pulmonary function or decreased ambient oxygen) or anemic anoxia (carbon monoxide-induced anoxia). Less common but still a significant syndrome is that of histotoxic anoxia (HCN). Use of the animal model makes it possible to determine if one of these syndromes is present and provides data necessary for a basic understanding of the mechanism. We have chosen to call the conditions producing the anoxic syndromes, with the exception of histotoxic anoxia, graded; and if a specific toxicant such as CO is responsible for the syndrome, to call that toxicant a graded toxicant. The term "graded" is used, because broadly variable levels of anoxia are responsible for a wide range of effects. The response of rats to CO has been previously investigated (*2*). The anoxic syndrome may result from the action of a single toxicant. Of course, a number of toxicants can be responsible for the same syndrome. Chemical analysis of combustion products and toxicological studies of the animal tissue may reveal the offending toxi-

cant. It must be emphasized that a number of factors may alter the intensity of the syndrome, but its basic qualitative nature will remain unchanged.

A specific organ or system may be affected, and animal monitoring during the course of intoxication may detect such alterations occurring independently of any effect which might be explained on the basis of any of the anoxic syndromes mentioned above. This emphasizes the importance of reference data relevant to the anoxic syndrome. Muscular paralysis, seizures, cardiac arrhythmia, etc., may occur as the consequence of the presence of a compound which has a high biological activity, i.e., produces its effect at very low concentrations. Most notably, such effects may be very serious, and the slope of th dose-response curve may be very high. Such toxicants have been termed limiting toxicants, since survival, defined in one of several ways, is limited by such toxicants, the action of which generally far outweighs the action of the graded toxicants. From the nature of the effects produced, pharmacological reference data, and chemical analysis of both the combustion products and toxicants present in tissue, it may be possible to identify the toxicant reponsible for a given unique effect.

Conditions Which Change the Qualitative Nature of the Intoxication Syndrome

Because of qualitative changes in the combustion products which occur as conditions of decomposition change, it is necessary to conduct experiments to determine whether the intoxication syndrome also changes. A range of heat fluxes representing realistic conditions of combustion should be selected, both flaming and nonflaming modes (with and without pilot light, respectively) should be used. The geometric configuration of the material and its physical form may also be important. In a practical sense, all factors which can be responsible for producing qualitative changes in combustion products should be investigated with respect to their influence upon the nature of the intoxication syndrome.

The production of any given syndrome may depend upon the presence of only a single compound, despite considerable qualitative alteration in the combustion products. On the other hand, changes in the heat flux may completely eliminate such compounds, resulting in a major alteration in the intoxication syndrome. Only by performing an empirical experiment and by use of an animal model is it possible to determine whether or not the intoxication syndrome can be changed by variation of these parameters.

Production of the Syndrome by Use of Synthetic Gas Mixtures and Selected Limiting Toxicants

The intoxication syndrome may be duplicated by selection of one or more of the combustion products produced under specific conditions of combustion and used to make up a synthetic gas mixture. In order to reproduce the syndrome it may be necessary to add particulates or aerosols. The syndrome may be intensified by such additions but not altered qualitatively. However, it is possible that the physical state of the combustion products may be critical in the production of a given syndrome. The ability to reproduce a syndrome with an artificial mixture is helpful in further identifying the substances primarily responsible for the syndrome.

Severity of Intoxication

In our opinion, the degrees of intoxication which should be investigated are those which are compatible with survival, rather than those which produce death. We have examined three levels of intoxication which we believe conform to this philosophy. The first level is loss of a conditioned avoidance response. This is a behavioral measure which requires the normal functioning of memory as well as the integration of sensory and effector components of the nervous system to elicit an escape response (*3*). The second level is that of ischemic anoxia or shock, at which point in the course of intoxication it becomes impossible to resuscitate the victim if the condition of intoxication is not reversed immediately. The third level of intoxication is that which relates to morbidity following acute intoxication. Assessment of animal function, particularly that of the central nervous system, must be made over a 2-week or longer period following exposure. Detailed evaluation must be directed at organs or systems which seem to exhibit prolonged periods of dysfunction following exposure.

The intensity of the exposure can be increased by increasing the concentration of essential toxicants in an artificial mixture until

intoxication levels one and two are reached. Level three is evaluated by careful follow-up examination. The mass of material and heat flux required to produce the various levels of intoxication (levels of toxicants) can then be calculated. In practice it may not be possible to produce such concentrations during actual material combustion, so that the resultant figure may be entirely theoretical. However, this value may have use in determination of relative toxicity.

Ideally, the intensity of exposure should be increased by first increasing the mass of material combusted. Care must be taken to assure that no qualitative change in the intoxication syndrome occurs as a consequence of physical factors which may alter qualitatively the composition of the combustion products. The intensity of exposure should be increased until levels one and two are reached. More refined measurement should then be introduced in order to determine the time-to-loss-of-function. If the modified National Bureau of Standards (NBS) exposure chamber or a smaller chamber is used, then the time required for smoke obscuration, the time to reach maximal optical density, may be included in the overall exposure time. Comparisons of the intoxication syndromes produced by different materials can be made only when identical combustion conditions and exposure chambers are used.

Proposal for the Assessment of Relative Toxicity

Once a description of the intoxication syndrome is complete and the involvement of various organs and systems has been described, then it is possible to approach the problem of comparing materials with respect to their toxicity. If two different materials produce qualitatively different intoxication syndromes, then comparison must be based upon some common reference point (it is not possible to compare quantitatively two generically different objects). Evaluation of combustion product toxicity by determining conditions which produce a significant intoxication endpoint may provide such a common reference point. In this regard the focus is upon the sign of intoxication rather than the mechanism by which the endpoint is reached. At intoxication level one, loss of the avoidance response, any one of a great many mechanisms ranging from neuromuscular paralysis to loss of cerebral function may be responsible. Considering the acute survival of the victim, it matters only that the response is lost.

By using a common intoxication endpoint, it is then possible to determine the mass of material, heat flux, and time required to produce this endpoint. A material which produces a substance with relatively high biological activity responsible for the intoxication syndrome will require a relatively small mass to do so. Confidence limits for production of the intoxication endpoint described in terms of mass, heat flux, and exposure time can be used to describe the toxicity of material and to compare it with other materials.

When the intoxication syndromes produced by two different materials are identical (and in the simplest case the syndromes do not vary as a function of the conditions of decomposition), then it will be possible to compare the intoxication produced by the materials with respect to any or all components of the syndrome, as for example the degree of CO-induced anoxia. This set of conditions comprises the simplest basis for comparison, and traditionally the anoxic state (CO-induced anoxia) has been the basis for comparison. Unfortunately, the syndrome of CO-induced anoxia accounts for only a portion of the intoxication syndromes that have been observed.

Of considerable importance to the producers and users of materials is identification of those materials which produce unique and severe toxicity. A rank ordering of materials on the basis of the "severity" of the syndrome produced can be attempted. Again applying the principle of "survival" as a guide, such factors as the dose–response relationship, i.e., slope of the dose–response curve, acute and chronic reversibility of effects, effect upon vital functions, rapidity of development of intoxication, availability of treatment for intoxication, and other factors can be considered. General material use and flammability characteristics will already have been considered prior to the evaluation of toxicity. However, these characteristics can modify significantly the relative importance of the assessment of toxicity. On the one hand, a material used in a manner which presents no threat to human life during decomposition may have a high level of toxicity and still be acceptable, provided no significant toxic threat is presented during manufacture. On the other hand, materials used in close proximity to humans

and in situations in which there is little chance of escape, as in aircraft, should conform to relatively high standards of structure, flammability, and toxicity.

A suggested hierarchy of intoxication syndromes might read as follows, in ascending order of severity:

(1) Reversible, nonvital organ or system effects
(2) Anoxic anoxia
(3) Anemic anoxia (CO-induced anoxia)
(4) Reversible vital organ-system effects
(5) Irreversible vital organ-system effects
(6) Histotoxic anoxia

This suggested hierarchy of intoxication, stated another way, indicates that reversible, nonvital effects, such as skin irritation, parenchymatous organ involvement, or neuromuscular blockade, are most acceptable. Next in order are the reversible anoxic states produced by of intoxication are produced over a wide range graded toxicants in which a number of levels of toxicant concentration. Finally, and most toxic, are those effects upon vital organ systems which are irreversible. These would include effects upon heart and brain function. Histotoxic anoxia is in the latter category, since it produces rapid impairment of vital functions, which is extremely difficult to reverse.

Materials which produce effects in categories (4) and (5) should be identified and segregated out, either for special application or discontinued use. Ideally, such categorization should be made prior to manufacture and use of these materials.

Examples of Intoxication Syndromes and Materials Which Produce Them

Response to a Phenolphthalein Polycarbonate Foam: Graded Toxicant Syndrome

Seventeen experiments were performed with one male 250 g Long-Evans rat in each experiment by use of the "static" chamber, a 40-liter acrylic glass-lined box. The rats were obtained from Simonsen Laboratories of Gilroy, California. Results are presented in Table 1. Fluxes of 2.5, 5.0, and 7.5 W/cm^2 were used to combust the material in both the flaming and nonflaming modes. At 5.0 and 7.5 W/cm^2 spontaneous ignition occurred. The syndrome produced on exposure to the combustion products was consistently one of CO-induced anoxia. Serum pH, bicarbonate, or excess base were not significantly affected until intoxication at shock levels was produced. Behavioral responses were those predicted from the degree of CO-induced anoxia present. Carboxyhemoglobin levels present when the conditioned avoidance response was lost were only slightly less than 50%. Increasing the mass of material combusted increased the level of carboxyemoglobin and the severity of the anoxia syndrome (Fig. 1). Varying heat fluxes or changing the combustion mode did not produce any qualitative change in the nature of the intoxication syndrome.

Examination of the remaining data in Table 1 reveals that the decrease in oxyhemoglobin can be accounted for by the elevation in carboxyemoglobin. The levels of pO_2 and pCO_2 indicate that pulmonary ventilation was adequate except when intoxication was severe enough to produce anoxic shock. In general, the loading of CO approached that seen during exposures using the pure gas. It is essential to know that hemoglobin and hematocrit (the percentage by volume of red blood cells in the blood) is normal, because rats with decreased oxygen-carrying capacity will not withstand

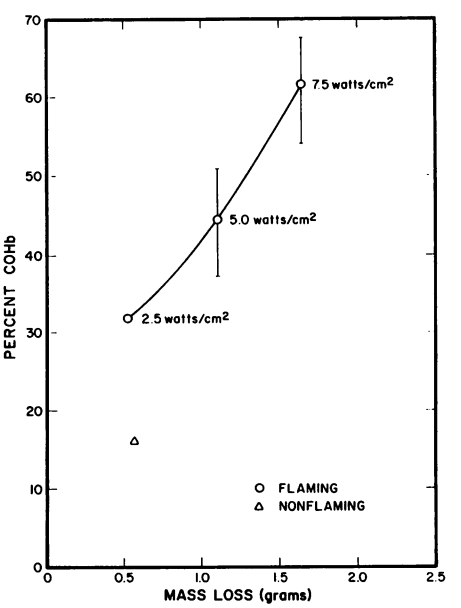

FIGURE 1. Carboxyhemoglobin levels following a 20-min exposure vs. mass of polyquinoxyline lost during combustion.

Table 1. Material A.

Animal	Time, sec	White blood count	Hematocrit	Oxyhemoglobin, g-%	Carboxyhemaglobin, g-%	Hemoglobin, g-%	pH	pCO_2	Base excess, meq/e	HCO_3^-	pO_2	O_2 Sat.	Flux, W/cm_2	Mass (final) / Mass (initial)
58	0	10.0	49.0	0	0	16.4	7.48	41.7	6.1	30.9	82.0	86.5	2.5	0.57/2.1[a]
	19	19.1	49.1	90.8	7.4	15.9	7.51	22.0	–2.0	17.6	105.	88.2	2.5	0.57/2.1[a]
59	0	23.3	41.9	84.6	0	15.0	7.44	38.6	2.0	26.0	74.	95.	2.5	0.57/2.1[a]
	24	15.9	33.3	85.7	11.8	11.7	7.49	29.5	1.2	22.4	72.	95.	2.5	0.57/2.1[a]
62	0	11.0	39.6	93.4	0	14.2	7.46	29.3	–1.1	20.7	74.0	95.4	2.5	0.57/2.1[a]
	17	15.7	41.3	87.6	7.5	15.7	7.55	18.6	–1.8	16.4	73.0	96.3	2.5	0.57/2.1[a]
64	0	9.4	38.3	84.4	26.5	13.4	7.51	35.7	5.1	28.5	72.0	95.5	2.5	0.57/2.1[a]
	20	29.3	37.4	62.2	36.6	13.2	7.55	25.4	1.	22.3	70.0	95.9	2.5	0.57/2.1[a]
63	0	17.6	35.2	98.2	0	12.3	7.47	16.9	–8.0	12.2	76.0	96.0	2.5	0.53/2.05[b]
	22	15.5	28.2	83.0	14.0	11.4	7.47	26.4	–2.2	19.1	70.0	94.9	2.5	0.53/2.05[b]
60	0	20.8	36.3	92.7	0	12.7	7.47	24.8	–3.2	17.9	81.0	96.5	2.5	0.53/2.05[b]
	22	8.5	33.2	47.4	40.9	11.6	7.48	28.9	–1.0	21.5	85.0	96.9	2.5	0.53/2.05[b]
66	0	12.7	39.5	89.2	11.0	14.3	7.47	29.2	–1.5	21.1	75.0	95.7	2.5	0.53/2.05[b]
	27	11.2	36.1	62.6	41.5	13.3	7.49	35.2	3.5	26.8	65.	93.9	2.5	0.53/2.05[b]
69	0	11.10	42.5	95.0	2.8	13.1	7.44	25.1	–4.8	16.9	64.3	93.9	2.5	0.53/2.05[b]
	22	13.3	27.6	68.0	32.	10.4	7.45	21.8	–6.5	15.0	60.8	94.0	2.5	0.53/2.05[b]
70	0	16.5	44.0	94.9	3.9	15.4	7.48	28.4	–1	21.1	73.	95.4	2.5	0.53/2.05[b]
	19	13.2	28.3	71.5	30.8	12.3	7.49	21.2	–6	20.7	63.	93.5	2.5	0.53/2.05[b]
53	0	14.8	44.9	95.6	10.	15.8	7.50	30.8	2.7	24.0	79.0	96.4	5	1.1/2.05[c]
	25	22.8	44.8	42.6	51.6	15.2	7.38	32.1	–4.8	18.7	75.0	94.6	5	1.1/2.05[c]
54	0	12.5	42.4	86.2	5.0	—	—	1.	—	—	—	—	5	1.1/2.05[c]
	21	12.0	37.5	45.3	48.	—	—	—	—	—	—	—	5	1.1/2.05[c]
55	0	9.6	47.6	95.2	0	—	—	—	—	—	—	—	5	1.1/2.05[c]
	20	12.0	27.1	43.2	39.4	9.8	7.52	20.6	–3.8	16.9	67.0	95.1	5	1.1/2.05[c]
56	0	8.0	45.9	88.1	–1.0	14.8	7.46	52.7	12.	37.3	59.0	90.6	5	1.1/2.05[c]
	22	9.7	37.2	64.7	37.5	13.3	7.24	34.6	–12.1	14.2	67.0	89.5	5	1.1/2.05[c]
71	0	16.0	34.4	89.4	3.00	12.3	7.46	29.1	–1.4	20.6	78.2	95.4	7.5	1.65/2.04[d]
	28	16.5	37.2	36.9	68.2	13.0	7.02	39.3	–20.4	9.7	22.1	17.0	7.5	1.65/2.04[d]
72	0	10.8	27.5	88.8	9.4	9.6	7.36	31.6	–6.2	17.5	68.0	92.5	7.5	1.65/2.04[d]
	18	—	44.1	40.3	54.3	15.1	7.16	49.5	–11.8	17.0	58.0	81.0	7.5	1.65/2.04[d]
73	0	—	43.1	90.5	.9	14.7	7.50	35.1	5.3	27.3	65.0	93.9	7.5	1.65/2.04[d]
	16	—	—	32.7	62.	—	—	—	—	—	—	—	7.5	1.65/2.04[d]
74	0	18.3	38.3	96.6	0	12.6	7.53	26.8	1.9	22.4	63.0	94.1	7.5	1.65/2.04[d]
	20	14.4	34.4	31.3	62.5	11.4	7.09	43.6	–17.9	12.7	74.0	88.1	7.5	1.65/2.04[d]

[a] Nonflaming; no intoxication.

[b] Flaming, spontaneous; no signs of intoxication.

[c] Flaming at 37 sec. Avoidance lost at 43% COHb; avoidance lost at 44%.

[d] Flaming at 5 sec. Avoidance lost 15 min into run. Intoxication effect at 8–12 min. Death at 18–25 min. COHb=61.8%.

the same elevation in carboxyhemoglobin levels as normal animals. Elevation in white blood cell count (WBC) may accompany the stress of the exposure. This did not seem to be a predominant effect. It is necessary to obtain all these values in order to detect other causes for anoxia, such as impairment of oxygen transport at the cellular level, or loss of oxygen-carrying capacity by red cell hemolysis.

Response to a Trimethylol Propane-Based Containing Fire Retardant Has Been Added: Polyurethane Foam to Which a Phosphate-Limiting Toxicant Syndrome

Three experiments were performed, one each at 2.5, 5.0, and 7.5 W/cm^2. There were four 250-300 g male Long-Evans rats in each experiment. Partway through the exposure animals were noted to convulse. All animals convulsed following removal from the chamber. At higher heat fluxes and with a greater percentage of material combusted, most of the animals died in convulsions. All behavioral responses were depressed as a consequence of the convulsions, but the startle reflex was enhanced prior to the development of seizures. Automatic, purposeful but inappropriate behavior was also seen. In "static box" experiments, spike and polyspike activity was noted in the electroencephalogram. Carboxyhemoglobin values were near control levels, and oxyhemoglobin levels were nearly normal. At all three fluxes this material produced a syndrome of epilepsy, grand mal seizures, and minor motor seizures. The syndrome can be distinguished clearly from that of an anoxic state.

Response to the Limiting Toxicant Responsible for Seizures

A bicyclic phosphate ester (BCPE) was subsequently discovered to be the toxicant responsible for the seizures (*4*). Preliminary experiments were carried out during which BCPE at a concentration of 1 mg/ml was injected intraperitoneally into unrestrained Long-Evans male rats in order to determine the dose of agent required for production of grand mal seizures. Following these preliminary investigations, 10 sling-restrained male Long-Evans rats, instrumented with epidural screw electrodes for recording of the electroencephalogram from frontal and occipital cortices, were then injected with aqueous solution of BCPE at a dose of 1 mg/kg. Animals were observed for the appearance of myoclonic jerks, grand mal seizures, and EEG abnormalities.

In a second series of experiments on five rats, the effect of BCPE on the performance of a conditioned avoidance response was studied and the loss of this response as a function of seizure activity was determined. In a 15-min preinjection training period, each rat learned to avoid a shock delivered to its left hind foot if the foot made contact with a metal plate placed a predetermined distance below the foot. The electric shock was delivered through two cutaneous electrodes attached to dorsal and ventral surfaces of the foot. By the end of the training period, most animals (in most larger groups >90%) made less than five lapses from avoidance per minute. Baseline EEG recording was also obtained in this period.

Preliminary experiments were carried out on one cat by intraperitoneal injections of BCPE at 1 mg/kg and 0.5 mg/kg separated by a time period of one week.

A 1 mg/kg dose of BCPE produced grand mal seizures in all animals. Seizures appeared within 2–5 min of injection. Unless interrupted by anticonvulsant medication such as phenobarbital, death following repeated grand mal seizures and status epilepticus ensued.

In the rats instrumented for conditioned avoidance response and EEG, a variable period of abrupt failure in avoidance preceded and followed the EEG evidence for seizure, defined as the production of cortical spike activity and marked reduction in frequency or amplitude, respectfully. Avoidance was lost when the EEG was still normal, i.e., prior to the development of a seizure. It was not difficult to detect the loss of avoidance, owing to the abrupt onset of lapses from avoidance. Prior to the first seizure, the time period during which avoidance was lost was quite variable, ranging from seconds to 0.5 min. In the period of postictal cortical depression, avoidance was recovered prior to the return of the EEG to normal. As seizures became more frequent and separated by periods of only 20–30 sec, the loss of avoidance became nearly continuous. In animals receiving a 1 mg/kg dose, death resulted from continued grand mal seizures.

A dose of 0.5 mg/kg produced cortical spiking in association with myoclonic jerking. Grand mal seizures occurred but were less se-

vere and did not become repetitive. Behavioral alterations consisted of licking, sialorrhea, and random purposeful movements, such as preening. Repetitive flexion jerks of the forelimbs occurred at a frequency of about five per second. During myoclonic jerks and a low frequency irregular cortical spike activity, avoidance was maintained.

In the cat, grand mal seizures were produced at a dose of 1 mg/kg, and these were preceded by a period lasting several minutes during which there was continuous vocalization, sialorrhea, licking, episodes of panting, piloerection on the tail, a "presenting" posture with the tail held erect, and movements suggesting great apprehension. At a dose of 0.5 mg/kg given to the same animal, one week later, similar abnormal behavior was produced, but no major seizures occurred.

Response to a Poly(vinyl Chloride) Foam

Twenty-three experiments were performed with one 250–300 g male Long-Evans rat in each experiment. Exposures were conducted in the "static box" during nonflaming combustion at 1.0 (2 rats), 1.5 (8 rats), and 2.5 (13 rats) W/cm². Lower heat fluxes were required for this material because of the severity of the intoxication syndrome produced at 5.0 W/cm² or above. As can be seen in Figures 2 and 3, the syndrome consists of acidosis associated with a mild to moderate increase in carboxyhemoglobin. Serum bicarbonate and base excess were significantly decreased—the findings being typical of metabolic acidosis. (Increases in carboxyhemoglobin of the order found here do not produce acidosis of this magnitude.) The acidosis was present at all heat fluxes used. More severe acidosis was found in rats exposed at higher heat fluxes and mass of material combusted, but considerable variability was found (Fig. 4).

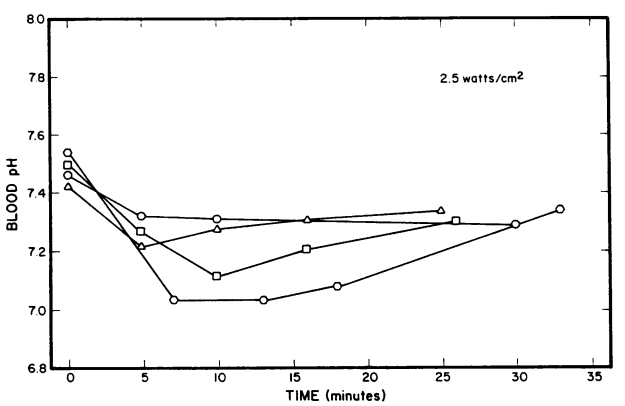

FIGURE 2. Arterial blood pH for individual rats vs. time during exposure to the combustion products of poly(vinyl chloride).

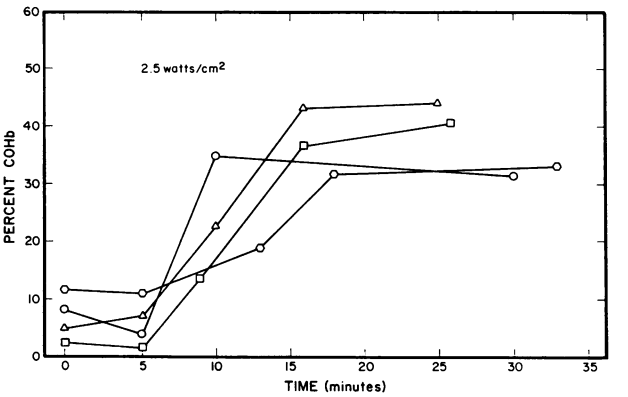

FIGURE 3. Arterial blood carboxyhemoglobin levels for individual rats vs. time during exposure to the combustion products of poly(vinyl chloride).

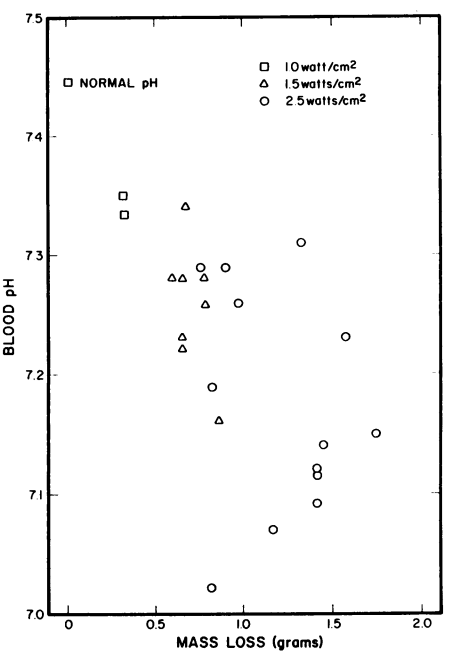

FIGURE 4. Lowest pH during exposure vs. mass lost in the combustion of poly(vinyl chloride).

More detailed analysis of the pH decrease and carboxyhemoglobin increase revealed that during the initial few minutes of exposure respiratory acidosis occurred. The pH decrease resulted from breath holding. Evidence for this was seen in the delayed rise of carboxyhemoglobin and normal serum bicarbonate levels during the first five minutes of exposure. When pH reached its lowest levels, a rise in carboxyhemoglobin occurred, and serum bicarbonate was significantly decreased. Measurement of respiratory rate confirmed this impression.

Rats sacrificed following exposure were found to have pulmonary edema and hemorrhage. Severe bronchial irritation was present. Pulmonary irritation and its consequences, impaired pulmonary ventilation, were a major feature of the syndrome.

Discussion

For any given material studied, the qualitative nature of the intoxication syndrome did not vary as a function of the heat flux or mode of combustion. The intensity of intoxication did vary up to a point, resulting in death at high heat fluxes and with greater amounts of material combusted. The fact that the qualitative nature of the intoxication syndrome did not vary with combustion conditions for these materials certainly does not obviate the need to examine other materials under varying conditions of thermal decomposition. The combustion products of a common material such as wood (Douglas fir) produces severe pulmonary irritation and anoxic anoxia at 2.5 W/cm^2, and CO-induced anoxia at 7.5 W/cm^2 in rats (*5*). Incomplete combustion of materials exposed to low heat fluxes may generate toxicants capable of producing severe and unique intoxication.

It is possible to describe an intoxication syndrome that is characteristic of a given material. This knowledge can be helpful in the identification of specific compounds responsible for organ or system effects. The early treatment at the fire scene of such effects such as severe metabolic acidosis could be life-saving. Recognition of specific intoxication syndromes in animals may facilitate their early recognition in men.

Conclusion

Intoxication syndromes of CO-induced anoxia, seizures, and CO-induced anoxia combined with metabolic acidosis have been defined in rats inhaling the combustion products of three different materials. It has been shown that the severity but not the quality of the intoxication syndrome varied as a function of condition of combustion. It is known that for some materials such as wood the intoxication syndrome does vary with conditions of combustion. These experiments suggest that various intoxication syndromes can be identified with certain materials. Such information can be useful in the medical treatment of fire victims and in the assessment of the relative toxicity of materials.

REFERENCES

1. 1976 Uniform Building Code, Proposed Research Committee Acceptance Criteria for Foam Plastics Under Section 1717; International Conference of Building Officials.
2. Petajan, J. H., et al. Sequelae of carbon monoxide-induced hypoxia in the rat. Arch. Neurol. 33: 152 (1976).
3. Einhorn, I. N. Physiological and toxicological aspects of smoke produced during the combustion of polymerica materials. Environ. Health Perspect. 11: 163 (1975).
4. Petajan, J. H., et al. Extreme toxicity of a fire retarded polyurethane foam. Science, 187: 742 (1975).
5. Packham, S. C., et al. Unpublished observations.